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THE EFFECT OF TEMPORARY OCCLUSION OF RENAL CIRCULATION ON RENAL FUNCTION *

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Of great importance in relation to the surgery of the kidney is the question concerning the length of time that the renal vessels may be clamped without permanent injury to renal function or renal tissue. The question is dealt with here experimentally. The renal vessels in rabbits and dogs have been clamped for varying periods of time, and subsequently renal function has been tested by the excretion of phenolsulphonephthalein, lactose, potassium iodid, salt and water. The presence or absence of albumin and casts in the urine has been observed. The results of such functional studies have been controlled by histological examination of the kidneys.

The effect of obstruction to the renal circulation on the urinary picture and the histology of the kidney has already been investigated. Robinson[1] showed that tying of the renal vein resulted in the appearance of albumin, blood, or both, in the urine, and in enlargement of the kidney. This has been confirmed by other observers. Paneth,[2] Munk[3] and de Souza[4] have shown that following ligation of the renal vein, the urine is small in amount. Ludwig[5] found that clamping the renal vessels for a period of minutes frequently interfered with the secretion of urine for hours. Heidenhain[6] found that on freeing the vessels after a temporary clamping the secretion of urine did not begin at once. Litten[7] observed after clamping both renal vessels for periods up to two hours, that the kidney became enlarged and congested. If the renal artery alone was tied for one-half or one hour, albumin and casts appeared in the urine. Pathologically, the tubules were affected as shown by their

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* For review of literature concerning partial or complete obstruction to renal circulation see our previous paper. Rowntree, Fitz and Geraghty: Studies of Renal Function in Experimental Chronic Passive Congestion, THE ARCHIVES INT. MED., 1913, xi, 121.

1. Robinson: Med. Chir. Tr., 1843, xxvi, 51.
2. Paneth: Pflüger's Arch., 1886, xxxix, 515.
3. Munk: Berl. klin. Wchnschr., 1864, i, 333.
4. De Souza: Jour. Physiol., 1900, xxvi, 139.
5. Ludwig Physiologie, 1856, ii, 416.
6. Heidenhain: Hermann's Handb. d. Physiol., 1883, v, Teil 1, 321.
7. Litten: Ztschr. f. klin. Med., 1880, p. 131.

inability to stain with indigo carmin. But such changes were temporary. If the artery was clamped for two hours, permanent injury occurred, evidenced by tubular necrosis with cast production, cellular infiltration, resulting in circumscribed scar formation with calcification.

Chirié and Mayer[8] after temporary clamping of both renal veins in dogs, noted, in four out of seven cases, death with convulsions. Carrel[9] was unable to confirm this observation.

Eisendrath and Strauss[10] have studied the pathological changes in the kidneys of rabbits after compressing the renal vessels for from fifteen to ninety minutes. According to their results, temporary compression — half an hour or less — caused slight damage. If longer, marked permanent lesions occurred in the parenchyma, as evidenced by interstitial cellular infiltration, coagulation necrosis of tubular epithelium, and later by the deposition of calcium in and about the destroyed epithelium.

Thus it has been shown that clamping of the renal vessels for periods up to an hour may produce temporary anuria, albuminuria and cylindruria. If interference with the renal circulation is maintained sufficiently long, permanent interstitial increase in tissue occurs in the kidney. Except for the amount of urine excreted and the presence in it of albumin or casts, no systematic study of renal function under such conditions has been made.

AUTHORS' EXPERIMENTS

In our experiments rabbits and dogs were etherized and the abdomen opened aseptically in the median line. The left kidney was exposed, and by careful blunt dissection the vessels were freed from the surrounding tissues. The artery and vein were raised on an artery forceps with as little stretching as possible and a small rubber protected bull-dog clamp placed around them. In each experiment it was noted that on the distal side of the forceps the artery did not pulsate, while the vein at once became distended; on the proximal side the vein was collapsed and the artery pulsated normally. No attempt was made to prevent the capsular circulation. After the left renal vessels were clamped, the right renal vessels were ligated. The right kidney was removed and weighed. In a few animals, for control, the right kidney was left untouched.

While the clamp was in place, the abdomen was closed and covered with a warm saline pad and towel. To try to obviate the factor of shock, the body heat was maintained. The animals were anesthetized as lightly as possible. After the desired interval of time had elapsed, the clamp was removed, the macroscopic appearance of the kidney noted, and

8. Chirié and Mayer: Compt. rend. Soc. de biol., 1907, i, 598.
9. Carrel: Compt. rend. d. Soc. de biol., 1909, i, 527.
10. Eisendrath and Strauss: Jour. Am. Med. Assn., 1910, lv, 2286; see also Guthrie: The Archives Int. Med., 1910, v, 232.

the peritoneum and abdomen sewn up. The bladder was then applied and the animals placed in metabolism cages. The clamp was applied in series of animals for ten, twenty, thirty, forty and sixty minutes. Repeated studies of renal function were made. Finally, the animals were killed, submitted to autopsy and the kidneys examined histologically after formaldehyd fixation, celloidin imbedding and hematoxylin and eosin staining.

TECHNIC OF TESTS OF RENAL FUNCTION

A short description of the various tests used for renal function, with their technic, is given.

The phthalein test was made according to the original technic of Rowntree and Geraghty.[11] One cubic centimeter of a phenolsulphonephthalein solution containing accurately 6 milligrams was injected aseptically into the leg muscles of the rabbits or lumbar muscles of the dogs, which were then placed in metabolism cages. The bladders were expressed or catheterized at the end of an hour and ten minutes, and the total urine for this time collected. The urine was made distinctly alkaline, diluted to 1 liter, and the amount of drug determined by the use of Rowntree and Geraghty's[12] modification of the Autenrieth-Königsberger colorimeter. In control animals it has been determined that the normal output in this time is 60 per cent. or more.

The lactose, potassium iodid, salt and water tests which have received a thorough study at the hands of Schlayer[13] and his co-workers and which we have used in relation to the renal function in experimental and clinical nephritides, were applied to this study.

From our previous work we feel that the mechanism of the excretion of lactose differs essentially from that of phthalein, salt and iodid. Throughout this investigation we have used it as an index of the condition of the vascular function[14] of the kidney, admitting that we need much more information concerning the manner and significance of its excretion.

The technic for the lactose test in rabbits has been identical with Schlayer's. One gram of lactose dissolved in 10 c.c. of distilled water was injected into the ear vein. The animals were placed in metabolism cages, the bladder expressed at the end of four hours and every hour thereafter up to eight hours. In dogs, according to our previous technic, 2 gm. were dissolved in 20 c.c. of water, and injected into the lumbar muscles.

Since the time necessary for total elimination has been considered by Schlayer of greater importance than the absolute amount recovered, and since our previous observations with lactose excretion agree with this, we have observed this exclusively. The presence of lactose in the urine was determined by Nylander's test, using similar amounts of urine, reagent and length of boiling time.

In rabbits under these conditions, the time necessary for the complete elimination of lactose is normally six hours or less and in dogs from four to six hours.

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11. Rowntree and Geraghty: Jour. Phar. and Exper. Therap., 1910, i, 579.

12. Rowntree and Geraghty: THE ARCHIVES INT. MED., 1912, ix, 284.

13. Schlayer: Deutsch. Arch. f. klin. Med., 1911, cii, 311; Schlayer and Takayasu: Deutsch. Arch. f. klin. Med., 1891, xcviii, 17; 1910, ci, 333.

14. For a review of the literature on this test and the others described below, see our previous paper. We have shown in a previous publication, however, that lactose is not excreted solely by the glomeruli.

According to the studies of Schlayer, potassium iodid is excreted by the tubules of the kidney, and on it he has placed most dependence in determining tubular functional capacity. In these studies 1 c.c. of a 2.5 per cent. solution has been administered intravenously to rabbits. For this the normal elimination time is twenty-four hours. In dogs, 0.5 gm. has been administered by mouth, which normally is excreted within sixty hours. The presence of the drug in the urine has been determined by Sandow's[15] test.

The excretion of salt following its administration in amounts greatly in excess of that ordinarily taken with the food is accomplished by the tubules, according to Schlayer. Normally, a large amount of salt is excreted by one of two methods. If it is given without extra water, it is almost entirely excreted within twenty-four hours without diuresis by increased salt concentration in the urine; if given with an excess of water, it is excreted partially through increased concentration in the urine and partially through diuresis.

Where vascular injury to the kidney exists, the simple administration of salt may be followed by a marked diuresis, all of the salt being excreted in twenty-four hours without its percentage content in the urine being at all increased. This is usually associated with a somewhat low and fixed specific gravity and the syndrome is spoken of as "vascular hypothenuria." Here the inability to concentrate is not due to any incapacity of the tubules to excrete salt, but to hypersensitive vessels which respond to the salt administration with a diuresis. In more severe vascular injury the vessels do not act in the same way, oliguria characterizing the urinary picture. In severe tubular destruction, a urine of fixed low specific gravity is obtained, the quantity of which is not materially affected by the administration of extra amounts of salt, and the salt content of which is not augmented by administration of extra amounts of salt because of the inability of the tubules to excrete it. Such a condition is known as "tubular hyposthenuria."

In these studies gm. 1.50 were given by stomach-tube to the rabbits, and gm. 3 to dogs. The urine for the following twenty-four hours was collected, and the salt concentration and absolute excretion estimated by the Lütke-Martius[16] method.

Finally, in order to make conditions as constant as possible, the rabbits were given 100 c.c. of water daily by stomach-tube. In addition,

15. Sandow's method consists in adding 1 c.c. of 2 per cent. sodium nitrite solution and 1 c.c. of 10 per cent. H_2SO_4 to from 10 to 30 c.c. of urine, followed by the addition of a small amount of chloroform. This is shaken together and allowed to separate into layers, the presence of the iodid being indicated by a purplish red or violet color in the chloroform.

16. Sahli: Lehrbuch der klinischen untersuchungs, Methoden, Franz Deuticke, Leipzig and Wien, 1899, p. 421.

they were allowed to eat green vegetables *ad libitum*. This produced a constant polyuria. Hence the amounts of urine were not followed from day to day. The dogs were allowed 300 c.c. of water daily, and were fed on meat when able to retain liquid or solid food. The lactose, phthalein and iodid tests were given synchronously since their excretion, and quantitative determination do not interfere with each other. In dogs, lactose and phthalein were given at the same time, but into the muscles of opposite sides.

Single catheter or expressed specimens of urine were taken from day to day. Albumin was tested by the nitric acid method. The sediment of centrifuged urine was examined microscopically for blood or casts.

As previously, in these studies we have considered the excretion of lactose as an index of vascular functional capacity; that of phthalein as an index of total renal function (though predominantly tubular), and the excretion of salt and iodid as an index of tubular functional capacity.

The results of these studies are shown in the accompanying protocols.[17]

PROTOCOLS OF EXPERIMENTS

I. Animals with one kidney removed, renal circulation clamped for 10 minutes.

RABBIT 1.—Body weight 1,650 gm. Weight of removed kidney 4.9 gm. Weight of remaining kidney at death 6.5 gm.

Sulphonephthalein excretion second day after operation 37 per cent.
Sulphonephthalein excretion third day after operation 62 per cent.
Sulphonephthalein excretion fifth day after operation 53 per cent.
Sulphonephthalein excretion seventh day after operation 58 per cent.
Lactose excretion first day after operation 6-7 hours.
Lactose excretion fourth day after operation 6-7 hours.
Iodid excretion first day after operation 36 hours +.
Iodid excretion fifth day after operation 36 hours +.
Salt excretion third day after operation 1.00 per cent. (1.20 gm.)
Salt excretion sixth day after operation 1.30 per cent. (1.00 gm.)

Albumin present for four days. Rare hyaline casts found until the seventh day. Animal killed on the eighth day.

RABBIT 2.—Weight 1,250 gm. Weight of removed kidney 4.6 gm. Weight of remaining kidney at death 4.5 gm.

Sulphonephthalein excretion second day after operation 65 per cent.
Sulphonephthalein excretion fourth day after operation 65 per cent.
Sulphonephthalein excretion fifth day after operation 62 per cent.
Sulphonephthalein excretion seventh day after operation 65 per cent.
Lactose excretion first day after operation 6 hours.
Lactose excretion fourth day after operation 7½ hours.
Lactose excretion seventh day after operation 5 hours.
Iodid excretion first day after operation 30 hours.
Iodid excretion fourth day after operation 24 hours.
Iodid excretion seventh day after operation 36 hours.

17. In addition seven rabbits were used, one with circulation clamped for ten minutes, three for thirty minutes, and two for forty minutes. All died within sixteen hours of operation. Realizing the individual variation in susceptibility and vitality of rabbits, it seemed fair to exclude these animals from their appropriate tables, especially as all had been deeply anesthetized, all but one had made poor ether recoveries, and one rabbit at operation had suffered from a severe hemorrhage due to trauma of the liver.

Salt excretion third day after operation 1.25 per cent. (1.00 gm.)
Salt excretion sixth day after operation 1.3 per cent. (1.3 gm.)

Albumin present for six days. Sediment negative throughout the experiment. Animal found dead on the eighth day. No cause found.

RABBIT 3.—Weight 2,250 gm. Weight of removed kidney 6 gm. (approx.). Weight of remaining kidney at death 8 gm.

Sulphonephthalein excretion first day after operation 9 per cent.
Sulphonephthalein excretion second day after operation 24 per cent.
Sulphonephthalein excretion third day after operation 35 per cent.
Sulphonephthalein excretion sixth day after operation 62 per cent.
Sulphonephthalein excretion eighth day after operation, 80 per cent.
Lactose excretion first day after operation 8 hours +.
Lactose excretion sixth day after operation 6 hours.
Lactose excretion thirteenth day after operation 5 hours.
Iodid excretion first day after operation 30 hours.
Iodid excretion sixth day after operation 34 hours.
Salt excretion third day after operation .72 per cent. (1.35 gm.)
Salt excretion eighth day after operation .56 per cent. (1.40 gm.)

Albumin present for three days. Sediment showed rare hyaline casts on the thirteenth day. Hematuria for three days. The animal was killed on the fourteenth day.

II. Animals with one kidney removed. Renal circulation clamped for twenty minutes.

RABBIT 1.—Weight 1,800 gm. Weight of removed kidney 6.6 gm. Weight of remaining kidney at death 5.5 gm.

Sulphonephthalein excretion first day after operation 32 per cent.
Sulphonephthalein excretion third day after operation 43 per cent.
Sulphonephthalein excretion fifth day after operation 42 per cent.
Sulphonephthalein excretion thirteenth day after operation 48 per cent.
Sulphonephthalein excretion twentieth day after operation 37 per cent.
Lactose excretion first day after operation 7½ hours.
Lactose excretion fifth day after operation 6 hours.
Lactose excretion fourteenth day after operation 5 hours.
Lactose excretion twentieth day after operation 7 hours +.
Iodid excretion first day after operation 24 hours.
Iodid excretion fourteenth day after operation 24 hours.
Iodid excretion twentieth day after operation 24 hours.
Salt excretion third day after operation 1.00 per cent. (1.1 gm.)
Salt excretion seventh day after operation .8 per cent. (2.00 gm.)
Salt excretion sixteenth day after operation .7 per cent. (1.6 gm.)

Albumin present for seven days. Few hyaline casts found until the seventh day. Hematuria for five days. Animal found dead on the twenty-seventh day. Histologically the kidney not remarkable.

RABBIT 2.—Weight 1,720 gm. Weight of removed kidney 6.4 gm. Weight of remaining kidney at death 6.5 gm.

Sulphonephthalein excretion first day after operation 27 per cent.
Sulphonephthalein excretion fifth day after operation 32 per cent.
Sulphonephthalien excretion sixth day after operation 60 per cent.
Sulphonephthalien excretion fourteenth day after operation 58 per cent.
Sulphonephthalien excretion twentieth day after operation 58 per cent.
Sulphonephthalein excretion twenty-eighth day after operation 64 per cent.
Lactose excretion first day after death 7½ hours.
Lactose excretion fifth day after operation 7 hours.
Lactose excretion fourteenth day after operation 5 hours.
Lactose excretion twenty-eighth day after operation 5 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion fifth day after operation 30 hours.
Iodid excretion fourteenth day after operation 24 hours.
Iodid excretion twenty-eighth day after operation 24 hours.
Salt excretion third day after operation .6 per cent. (1.1 gm.).
Salt excretion seventh day after operation 1.2 per cent. (1.8 gm.).

Salt excretion sixteenth day after operation .53 per cent. (1.3 gm.).
Salt excretion twenty-eighth day after operation .46 per cent. (2.00 gm.).

Albumin present for three days. Hematuria for four days. No casts found after the fifth day. Animal killed the twenty-eighth day.

RABBIT 3.—Weight 2,020 gm. Weight of removed kidney 6.5 gm. Weight of remaining kidney at death 7.00 gm.

Sulphonephthalein excretion first day after operation 55 per cent.
Sulphonephthalein excretion third day after operation 35 per cent.
Sulphonephthalein excretion fifth day after operation 65 per cent.
Sulphonephthalein excretion fifteenth day after operation 64 per cent.
Sulphonephthalein excretion twenty-eighth day after operation 70 per cent.
Lactose excretion first day after operation 7½ hours.
Lactose excretion fifth day after operation 4 hours.
Lactose excretion fifteenth day after operation 4 hours.
Lactose excretion twenty-third day after operation 6 hours
Iodid excretion first day after operation 24 hours.
Iodid excretion fifth day after operation 24 hours.
Iodid excretion twenty-third day after operation 24 hours.
Salt excretion third day after operation 1.00 per cent. (1.1 gm.).
Salt excretion twelfth day after operation .8 per cent. (2.4 gm.).

Albumin present for three days. Hematuria for one day. No casts found after the sixth day. Animal killed the twenty-eighth day.

DOG 1.—Weight 5 kilos. Weight of the removed kidney 20 gm.

Sulphonephthalein excretion first day after operation 40 per cent.
Sulphonephthalein excretion second day after operation 60 per cent.
Sulphonephthalein excretion fifth day after operation 50 per cent.
Sulphonephthalein excretion ninth day after operation 68 per cent.
Sulphonephthalein excretion twelfth day after operation 60 per cent.
Lactose excretion first day after operation 8 hours +.
Lactose excretion fifth day after operation 8 hours.
Lactose excretion ninth day after operation 5 hours.
Iodid excretion second day after operation 48 hours.
Iodid excretion twelfth day after operation 48 hours.
Salt excretion second day after operation .85 per cent. (3.00 gm.).

Albumin present for one day. No casts found after the second day. The animal was allowed to live, since he had made an apparently normal recovery.

III.—Animals with one kidney removed; renal circulation clamped for thirty minutes.

RABBIT 1.—Weight 1,700 gm. Weight of removed kidney 5 gm. (Approx.) Weight of remaining kidney after death 6.5 gm.

Sulphonephthalein excretion first day after operation 46 per cent.
Sulphonephthalein excretion second day after operation 40 per cent.
Sulphonephthalein excretion fourth day after operation 60 per cent.
Sulphonephthalein excretion thirteenth day after operation 67 per cent.
Sulphonephthalein excretion twenty-eighth day after operation 72 per cent.
Sulphonephthalein excretion thirty-first day after operation 60 per cent
Lactose excretion first day after operation 6½ hours.
Lactose excretion fourth day after operation 5 hours.
Lactose excretion thirteenth day after operation 5 hours.
Lactose excretion twenty-eighth day after operation 5 hours.
Iodid excretion first day after operation 36 hours.
Iodid excretion fourth day after operation 30 hours.
Iodid excretion thirteenth day after operation 24 hours.
Salt excretion third day after operation 1.3 per cent. (1.7 gm.).
Salt excretion sixth day after operation .8 per cent. (1.4 gm.).
Salt excretion thirty-first day after operation .9 per cent. (1.4 gm.).

Albuminuria for four days. No casts found after the thirteenth day. Animal killed on the thirty-first day.

RABBIT 2.—Weight 2,400 gm. Weight of removed kidney 7.6 gm. Weight of remaining kidney after death 11.5 gm.

Sulphonephthalein excretion first day after operation 36 per cent.
Sulphonephthalein excretion second day after operation 40 per cent.
Sulphonephthalein excretion fourth day after operation 70 per cent.
Sulphonephthalein excretion fifteenth day after operation 62 per cent.
Lactose excretion first day after operation 7 hours +.
Lactose excretion fourth day after operation 5 hours.
Lactose excretion fifteenth day after operation 5 hours.
Iodid excretion fifteenth day after operation 24 hours.
Salt excretion first day after operation .7 per cent. (1.6 gm.).
Salt excretion fifteenth day after operation .6 per cent. 2.4 gm.).

Albumin present for one day. Hematuria for two days. No casts found after the fourth day. Animal killed the fifteenth day.

RABBIT 3.—Weight 2.600 gm. Weight of removed kidney 9.6 gm. Weight of remaining kidney after death 8 gm.

Sulphonephthalein excretion second day after operation 55 per cent.
Sulphonephthalein excretion fourth day after operation 70 per cent.
Sulphonephthalein excretion fifteenth day after operation 80 per cent.
Sulphonephthalein excretion twentieth day after operation 74 per cent.
Lactose excretion first day after operation 7 hours.
Lactose excretion fourth day after operation 5 hours.
Lactose excretion fourteenth day after operation 7 hours.
Lactose excretion twentieth day after operation 5 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion fourth day after operation 24 hours.
Iodid excretion fifteenth day after operation 24 hours.
Salt excretion third day after operation 1.1 per cent. (2.5 gm.).
Salt excretion fourteenth day after operation .52 per cent. (2.1 gm.).
Salt excretion twentieth day after operation .65 per cent. (1.9 gm.).

Albumin present for one day. Hematuria for one day. No casts seen after the third day. Animal killed the thirtieth day.

DOG 1.—Weight 7 kilos. Weight of removed kidney 24 gm.

Sulphonephthalein excretion second day after operation 36 per cent.
Sulphonephthalein excretion third day after operation 52 per cent.
Sulphonephthalein excretion fifth day after operation 55 per cent.
Lactose excretion third day after operation 8 hours.
Iodid excretion second day after operation 48 hours.
Salt excretion third day after operation 1 per cent. (1.6 gm.).

Albumin for two days. Casts found on the fifth day. Animal made an uneventful recovery and allowed to live.

IV.—Animal with one kidney removed: renal circulation clamped for forty minutes.

RABBIT 1.—Weight 2.070 gm. Weight of removed kidney 5.7 gm. Weight of remaining kidney after death 7.2 gm.

Sulphonephthalein excretion first day after operation 24 per cent.
Sulphonephthalein excretion second day after operation 46 per cent.
Sulphonephthalein excretion third day after operation 50 per cent.
Sulphonephthalein excretion fourth day after operation 62 per cent
Sulphonephthalein excretion eighth day after operation 70 per cent
Lactose excretion second day after operation 6 hours.
Lactose excretion eighth day after operation 6 hours.
Lactose excretion twelfth day after operation 5 hours.
Iodid excretion first day after operation 48 hours.
Salt excretion fourth day after operation 1 per cent. (1.5 gm.).
Salt excretion tenth day after operation .7 per cent. (1.2 gm.).

Albuminuria for eight days. Hematuria for one day. No casts found after the fourth day. Animal killed on the twelfth day on account of general infection.

RABBIT 2.—Weight 1.600 gm. Weight of removed kidney 4.6 gm. Weight of remaining kidney after death 6.5 gm.

Sulphonephthalein excretion first day after operation 46 per cent.
Sulphonephthalein excretion second day after operation 47 per cent.

Sulphonephthalein excretion third day after operation 56 per cent.
Lactose excretion first day after operation 8 hours +.
Lactose excretion third day after operation 7 hours +.
Iodid excretion first day after operation 30 hours.
Iodid excretion third day after operation 24 hours.
Salt excretion third day after operation 1 per cent. (1.2 gm.)

Albumin and casts present until death. Animal killed on the fourth day on account of general infection.

RABBIT 3.—Weight 2.200 gm. Weight of removed kidney 6.00 gm. Weight of remaining kidney after death 9.00 gm.

Sulphonephthalein excretion first day after operation 45 per cent.
Sulphonephthalein excretion second day after operation 54 per cent.
Sulphonephthalein excretion fourth day after operation 60 per cent.
Sulphonephthalein excretion fifth day after operation 70 per cent.
Lactose excretion first day after operation 8 hours.
Lactose excretion third day after operation 5 hours.
Lactose excretion fifth day after operation 4 hours.
Iodid excretion first day after operation 30 hours.
Iodid excretion third day after operation 24 hours.
Salt excretion second day after operation .9 per cent. (1.00 gm.)
Salt excretion fifth day after operation .9 per cent. (2.5 gm.)

Albumin present for three days. Hematuria for one day. No casts seen after the fourth day. Animal killed on the sixth day.

RABBIT 4.—Weight 1,770 gm. Weight of removed kidney 5.00 gm. Weight of remaining kidney after death 7.00 gm.

Sulphonephthalein excretion first day after operation 15 per cent.
Sulphonephthalein excretion second day after operation 14 per cent.
Sulphonephthalein excretion third day after operation 8 per cent.
Lactose excretion first day after operation 8 hours +.
Lactose excretion third day after operation 6 hours.
Iodid excretion first day after operation 30 per cent.
Salt excretion second day after operation 1.00 per cent. (.7 gm.)

No albumin found after the second day. Hematuria for one day. Casts seen on the third day. Animal found dead on the fourth day with acute peritonitis.

RABBIT 5.—Weight 2.320 gm. Weight of removed kidney 7 gm. Weight of remaining kidney after death 10 gm.

Sulphonephthalein excretion first day after operation 47 per cent.
Sulphonephthalein excretion fourth day after operation 62 per cent.
Sulphonephthalein excretion twelfth day after operation 67 per cent.
Sulphonephthalein excretion fourteenth day after operation 70 per cent.
Lactose excretion second day after operation 6 hours.
Lactose excretion fourth day after operation 6 hours.
Lactose excretion thirteenth day after operation 5 hours.
Iodid excretion second day after operation 24 hours.
Salt excretion second day after operation .7 per cent. (1.3 gm.)
Salt excretion thirteenth day after operation .9 per cent. (2.5 gm.)

Albuminuria for two days. Casts present for four days. Animal killed on the fifteenth day.

DOG 1.—Weight 6 kilos. Weight of removed kidney 33 gm. Weight of remaining kidney after death 50 gm.

Sulphonephthalein excretion first day after operation traces.
Sulphonephthalein excretion second day after operation traces.
Sulphonephthalein excretion third day after operation traces.
Lactose excretion first day after operation 8 hours +.
Lactose excretion second day after operation 8 hours.
Salt and iodid not given. Albumin, blood and casts present until death.

Animal killed on the fourth day on account of extreme toxemia.

DOG 2.—Weight 10 kilos. Weight of removed kidney 30 gm.

Sulphonephthalein excretion first day after operation 20 per cent.
Sulphonephthalein excretion third day after operation 30 per cent

Sulphonephthalein excretion fourth day after operation 64 per cent.
Sulphonephthalein excretion seventh day after operation 68 per cent.
Lactose excretion first day after operation 8 hours +.
Lactose excretion fourth day after operation 8 hours +.
Lactose excretion seventh day after operation 6 hours.
Iodid excretion second day after operation 48 hours.
Salt excretion second day after operation .4 per cent. (.80 gm.)

Albumin present for four days. No casts seen after the fourth day. Animal made an uneventful recovery and allowed to live.

V.—Animals with one kidney removed; renal circulation clamped for one hour.

Rabbit 1.—Weight 1,750 gm. Weight of removed kidney 7 gm. Weight of remaining kidney after death 7.5 gm.

Sulphonephthalein excretion first day after operation 32 per cent.
Sulphonephthalein excretion third day after operation 35 per cent.
Lactose excretion second day after operation 8 hours +.
Iodid excretion second day after operation 2 hours +.
Salt excretion second day after operation .6 per cent. (.5 gm.)

Albumin and casts found on the third day. Hematuria for one day. Animal found dead on the fourth day. Autopsy showed acute peritonitis.

Rabbit 2.—Weight 2,000 gm. Weight of removed kidney 5.2 gm. Weight of remaining kidney after death 6.5 gm.

Sulphonephthalein excretion first day after operation 7 per cent.
Lactose excretion second day after operation 8 hours +.
Salt excretion second day after operation .7 per cent. (.8 gm.)

Albumin, casts and blood in the urine on the third day. Animal found dead.

Rabbit 3.—Weight 1,800 gm. Weight of removed kidney 6.00 gm. Weight of remaining kidney after death 9.00 gm. Animal died anuric in seventy-two hours.

Rabbit 4.—Weight 1,700 gm. Weight of removed kidney 7 gm. Weight of remaining kidney after death 9.5 gm.

Sulphonephthalein excretion first day after operation 9 per cent.
Sulphonephthalein excretion second day after operation 12 per cent.
Sulphonephthalein excretion third day after operation 20 per cent.
Sulphonephthalein excretion sixth day after operation 8 per cent.
Lactose excretion first day after operation 8 hours +.
Lactose excretion third day after operation 8 hours +.
Iodid excretion first day after operation 48 hours.
Salt excretion third day after operation .8 per cent. (2.1 gm.)

Albumin and casts present until death. Animal found dead a few days after last note. Phthalein excreted in traces, lactose markedly delayed.

Rabbit 5.—Weight 1,400 gm. Weight of removed kidney 4 gm. Weight of remaining kidney after death 9.5 gm.

Sulphonephthalein excretion first day after operation traces.
Sulphonephthalein excretion second day after operation traces.
Sulphonephthalein excretion third day after operation traces.
Lactose excretion first day after operation none recovered.

Albumin, blood and casts present until death on the fourth day. During the last twenty-four hours passed 10 c.c. of urine.

VI.—Animals in which the renal circulation has been clamped in one kidney for an hour, the other kidney being left untouched.

Rabbit 1.—Weight 1,650 gm. Weight of unclamped kidney at death 5.00 gm. Weight of clamped kidney at death 5.00 gm.

Sulphonephthalein excretion first day after operation 30 per cent.
Sulphonephthalein excretion second day after operation 52 per cent.
Sulphonephthalein excretion sixth day after operation 56 per cent.
Sulphonephthalein excretion eighth day after operation 75 per cent.
Sulphonephthalein excretion eighteenth day after operation 60 per cent.

Sulphonephthalein excretion twenty-second day after operation 70 per cent.
Sulphonephthalein excretion twenty-fifth day after operation 76 per cent.
Lactose excretion first day after operation 7 hours.
Lactose excretion fourth day after operation 6 hours.
Lactose excretion eighth day after operation 5 hours.
Lactose excretion fifteenth day after operation 6 hours.
Lactose excretion twenty-fifth day after operation 5 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion eighth day after operation 24 hours.
Iodid excretion twenty-second day after operation 24 hours.
Salt excretion sixth day after operation .5 per cent. (1.1 gm.).
Salt excretion twenty-fifth day after operation .76 per cent. (1.2 gm.)

Albumin present for two days. No casts found after the sixth day. Animal killed on the twenty-sixth day.

RABBIT 2.—Weight 2,200 gm. Weight of unclamped kidney at death 7.5 gm. (approx.). Weight of clamped kidney at death 7.5 gm.

Sulphonephthalein excretion first day after operation 59 per cent.
Sulphonephthalein excretion fifth day after operation 74 per cent.
Sulphonephthalein excretion seventeenth day after operation 78 per cent.
Lactose excretion third day after operation 6 hours.
Lactose excretion tenth day after operation 7 hours +.
Lactose excretion eighteenth day after operation 6 hours.
Iodid excretion third day after operation 24 hours.
Iodid excretion eighteenth day after operation 24 hours.
Salt excretion eighteenth day after operation .3 per cent. (1.20 gm.)

Albumin present for one day. No casts seen after the fifth day. Animal killed on the nineteenth day.

RABBIT 3.—Weight 1,700 gm.

Sulphonephthalein excretion first day after operation 50 per cent.
Sulphonephthalein excretion third day after operation 58 per cent.
Sulphonephthalein excretion seventh day after operation 70 per cent.
Lactose excretion third day after operation 6 hours.
Lactose excretion seventh day after operation 5 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion seventh day after operation 24 hours.
Salt excretion fifth day after operation .7 per cent. (1.4 gm.)

Albumin present for one day. Casts found on the seventh day. Animal found dead on the twelfth day. No cause found.

VII.—Animals in which one kidney has been removed, the circulation of the other being left untouched.

RABBIT 1.—Weight 1,900 gm. Weight of removed kidney 7 gm. Weight of remaining kidney after death 7.5 gm.

Sulphonephthalein excretion first day after operation 50 per cent.
Sulphonephthalein excretion second day after operation 65 per cent.
Sulphonephthalein excretion fifth day after operation 60 per cent.
Sulphonephthalein excretion ninth day after operation 70 per cent.
Lactose excretion first day after operation 5 hours.
Lactose excretion ninth day after operation 5 hours.
Lactose excretion sixteenth day after operation 6 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion sixteenth day after operation 24 hours.
Salt excretion third day after operation .5 per cent. (2.00 gm.)

Traces of albumin found for one day. Blood and casts found for one day. Animal killed on the twentieth day.

RABBIT 2.—Weight 2,200 gm. Weight of removed kidney 6 gm. Weight of remaining kidney after death 8.5 gm.

Sulphonephthalein excretion first day after operation 69 per cent.
Sulphonephthalein excretion second day after operation 70 per cent.
Sulphonephthalein excretion twelfth day after operation 75 per cent.
Sulphonephthalein excretion thirteenth day after operation 80 per cent.

Lactose excretion first day after operation 5 hours.
Lactose excretion thirteenth day after operation 5 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion thirteenth day after operation 24 hours.
Salt excretion third day after operation .3 per cent. (.7 gm.)
Salt excretion thirteenth day after operation .26 per cent. (1.1 gm.)
Albumin present for one day. No casts seen. Animal killed on the fourteenth day.

RABBIT 3.—Weight 1,850 gm. Weight of removed kidney 7 gm. Weight of remaining kidney after death 7 gm.
Sulphonephthalein excretion first day after operation 25 per cent.
Sulphonephthalein excretion second day after operation 30 per cent.
Sulphonephthalein excretion fifth day after operation 55 per cent.
Sulphonephthalein excretion twentieth day after operation 70 per cent.
Lactose excretion first day after operation 5 hours.
Lactose excretion nineteenth day after operation 5 hours.
Iodid excretion first day after operation 24 hours.
Iodid excretion nineteenth day after operation 24 hours.
Salt excretion third day after operation .6 per cent.
Salt excretion nineteenth day after operation 1.1 per cent. (1.5 gm.)
Albumin present for one day. Hematuria for one day. Animal killed on the twenty-first day.

Clamping of the renal circulation up to forty minutes, in the majority of cases, produced a definite disturbance in renal function. Its intensity bore no relation to the length of time the vessels were clamped, nor was the vascular or tubular function chiefly affected (Protocols I to IV). This was shown by the presence of albumin and casts in the urine, by a diminished phthalein output of varying degree, and by a delayed lactose and iodid excretion. Salt was constantly well excreted. The animals recovering, regained nearly normal function within six days, showing that the disturbance was slight and temporary. One animal failed to return to a normal phthalein output. No explanation was found for this at autopsy. Two animals with circulation clamped for forty minutes died quickly with marked signs of renal insufficiency.

All the animals, however, with one kidney removed and the circulation of the remaining kidney clamped for an hour (Protocol V) died within eight days. There was evidence clinically as well as by these tests of extreme disturbance of function. An interesting proof of how important a part in renal surgery the unoperated kidney plays is seen in Protocol VI. In this series, though the circulation was clamped for an hour, with a normal kidney remaining, the function was but slightly and temporarily disturbed.

That the effect of nephrectomy alone did not produce the results obtained is seen from Protocol VII. In two animals the functional tests were unaffected. In the third the phthalein output was slightly reduced for three days. The other tests were normal.

Pathologically, similar changes were noted to those described by previous authors. The earliest changes, grossly, were marked congestion with scattered minute hemorrhages. As the length of time following

the operation increased, the kidneys hypertrophied, but otherwise appeared normal.

Microscopically first were seen hemorrhage, edema, destruction of cells, as evidenced by poor staining, the presence of hyaline-like casts in the tubules, and foci of leukocytes, endothelial phagocytes and mononuclear cells between the tubules and around the glomeruli. In time the kidney regained nearly normal appearance. In a few kidneys there were areas of increased interstitial tissue, and rarely thickening of a few glomerular capsules. It was not possible to find any definite relationship between the anatomical changes and the disturbance of function, except that in those kidneys clamped for an hour there was more edema and necrosis than in the others. In none of the kidneys examined was there evidence of any progressive lesion. The changes were all acute or healed.

From these experiments on animals it seems clear that renal circulation may be clamped for at least forty minutes without danger of marked permanent damage to the kidney either histologically or functionally. How far these results are applicable to human surgery is an open question. From the fact that these experiments were made under the most disadvantageous conditions possible, that is, with only one functionating kidney, it would seem fair to assume that in man with one kidney normal, the circulation of the other kidney could be clamped for a considerable length of time without harm.

CONCLUSIONS

1. In rabbits and dogs with one kidney removed, the circulation of the other kidney may be clamped for as long a time as forty minutes with recovery. If the renal circulation is clamped for a longer time, the animals die with signs of renal insufficiency.

2. In animals with the circulation clamped for not longer than forty minutes, temporary disturbance in renal function is produced as shown by the presence of albumin and casts in the urine, by a diminished phthalein output and by a delayed lactose and iodid excretion. Normal function is regained within six days.

3. Acute or healed pathological changes are found in kidneys so treated. The acute changes consist of edema, hemorrhage, necrosis and cellular infiltration. The healed changes consist in foci of connective tissue. No progressive lesion is found.

4. Except in the most extreme cases, there is no definite relation demonstrable by the functional tests used between the pathological and functional disturbances produced.

5. In rabbits with one normal kidney, the circulation of the other kidney may be clamped for at least an hour without permanent injury to the animal's general condition or renal function.